Claims

1. A method for treating or preventing an infectious disease in a subject having or at risk of developing the infectious disease, comprising

administering to a subject in need of such treatment a poly-G nucleic acid and an anti-microbial agent in an effective amount for treating or preventing the infectious disease,

wherein the poly-G nucleic acid is not conjugated to the anti-microbial agent.

2. The method of claim 1, wherein the effective amount is a synergistic amount.

3. The method of claim 1, wherein the poly-G nucleic acid comprises the following formula:

5' $X_1X_2GGGX_3X_4$ 3'

wherein X_1, X_2, X_3, and X_4 are nucleotides.

4. The method of claim 3, wherein at least one of X_3 and X_4 are a G.

5. The method of claim 3, wherein both of X_3 and X_4 are a G.

6. The method of claim 1, wherein the poly-G nucleic acid comprises the following formula:

5' GGGNGGG 3'

wherein N represents between 0 and 20 nucleotides.

7. The method of claim 1, wherein the poly-G nucleic acid comprises the following formula:

5' GGGNGGGNGGG 3' (SEQ ID NO: 134)

wherein N represents between 0 and 20 nucleotides.

8. The method of claim 1, wherein the poly-G nucleic acid is administered mucosally.

9. The method of claim 8, wherein the poly-G nucleic acid is free an unmethylated CpG motif.

10. The method of claim 9, wherein the poly-G nucleic acid is selected from the group consisting of SEQ ID NOs: 95-133.

11. The method of claim 1, wherein the poly-G nucleic acid is administered systemically.

12. The method of claim 11, wherein the poly-G nucleic acid includes at least one unmethylated CG dinucleotide.

13. The method of claim 12, wherein the poly-G nucleic acid is selected from the group consisting of SEQ ID NO 46, 47, 58, and 61.

14. The method of claim 1, wherein the anti-microbial agent is selected from the group consisting of an anti-bacterial agent, an anti-viral agent, an anti-fungal agent, and an anti-parasitic agent.

15. The method of claim 14, wherein the anti-viral agent is selected from the group consisting of immunoglobulin, amantadine, interferon, nucleoside analogues, and protease inhibitors.

16. The method of claim 14, wherein the antiviral agent is selected from the group consisting of Acemannan; Acyclovir; Acyclovir Sodium; Adefovir; Alovudine; Alvircept Sudotox; Amantadine Hydrochloride; Aranotin; Arildone; Atevirdine Mesylate; Avridine; Cidofovir; Cipamfylline; Cytarabine Hydrochloride; Delavirdine Mesylate; Desciclovir; Didanosine; Disoxaril; Edoxudine; Enviradene; Enviroxime; Famciclovir; Famotine Hydrochloride; Fiacitabine; Fialuridine; Fosarilate; Foscarnet Sodium; Fosfonet Sodium; Ganciclovir; Ganciclovir Sodium; Idoxuridine; Kethoxal; Lamivudine; Lobucavir; Memotine Hydrochloride; Methisazone; Nevirapine; Penciclovir; Pirodavir; Ribavirin; Rimantadine Hydrochloride; Saquinavir Mesylate; Somantadine Hydrochloride; Sorivudine; Statolon; Stavudine; Tilorone Hydrochloride; Trifluridine; Valacyclovir Hydrochloride; Vidarabine; Vidarabine Phosphate; Vidarabine Sodium Phosphate; Viroxime; Zalcitabine; Zidovudine; and Zinviroxime.

17. The method of claim 14, wherein the anti-bacterial agent is an antibiotic.

18. The method of claim 14, wherein the anti-bacterial agent is a broad spectrum antibiotic.

19. The method of claim 14, wherein the anti-bacterial agent is a narrow spectrum antibiotic.

20. The method of claim 14, wherein the anti-bacterial agent is a limited spectrum antibiotic.

21. The method of claim 14, wherein the anti-bacterial agent is selected from the group consisting of cell wall synthesis inhibitors, cell membrane inhibitors, protein synthesis inhibitors, nucleic acid synthesis or functional inhibitors, and competitive inhibitors.

22. The method of claim 14, wherein the anti-bacterial agent is selected from the group consisting of natural penicillins, semi-synthetic penicillins, clavulanic acid, cephalolsporins, bacitracin, ampicillin, carbenicillin, oxacillin, azlocillin, mezlocillin, piperacillin, methicillin, dicloxacillin, nafcillin, cephalothin, cephapirin, cephalexin, cefamandole, cefaclor, cefazolin, cefuroxine, cefoxitin, cefotaxime, cefsulodin, cefetamet, cefixime, ceftriaxone, cefoperazone, ceftazidine, moxalactam, carbapenems, imipenems, monobactems, euztreonam, vancomycin, polymyxin, amphotericin B, nystatin, imidazoles, clotrimazole, miconazole, ketoconazole, itraconazole, fluconazole, rifampins, ethambutol, tetracyclines, chloramphenicol, macrolides, aminoglycosides, streptomycin, kanamycin, tobramycin, amikacin, gentamicin, tetracycline, minocycline, doxycycline, chlortetracycline, erythromycin, roxithromycin, clarithromycin, oleandomycin, azithromycin, chloramphenicol, quinolones, co-trimoxazole, norfloxacin, ciprofloxacin, enoxacin, nalidixic acid, temafloxacin, sulfonamides, gantrisin, and trimethoprim.

23. The method of claim 14, wherein the anti-bacterial agent is selected from the group consisting of Acedapsone ; Acetosulfone Sodium; Alamecin; Alexidine; Amdinocillin; Amdinocillin Pivoxil; Amicycline; Amifloxacin; Amifloxacin Mesylate; Amikacin; Amikacin

Sulfate; Aminosalicylic acid; Aminosalicylate sodium; Amoxicillin; Amphomycin; Ampicillin; Ampicillin Sodium; Apalcillin Sodium; Apramycin; Aspartocin; Astromicin Sulfate; Avilamycin; Avoparcin; Azithromycin; Azlocillin; Azlocillin Sodium; Bacampicillin Hydrochloride; Bacitracin; Bacitracin Methylene Disalicylate; Bacitracin Zinc; Bambermycins; Benzoylpas Calcium; Berythromycin ; Betamicin Sulfate; Biapenem; Biniramycin; Biphenamine Hydrochloride ; Bispyrithione Magsulfex ; Butikacin; Butirosin Sulfate; Capreomycin Sulfate; Carbadox; Carbenicillin Disodium; Carbenicillin Indanyl Sodium; Carbenicillin Phenyl Sodium; Carbenicillin Potassium; Carumonam Sodium; Cefaclor; Cefadroxil; Cefamandole; Cefamandole Nafate; Cefamandole Sodium; Cefaparole; Cefatrizine; Cefazaflur Sodium; Cefazolin; Cefazolin Sodium; Cefbuperazone; Cefdinir; Cefepime; Cefepime Hydrochloride; Cefetecol; Cefixime; Cefmenoxime Hydrochloride; Cefmetazole; Cefmetazole Sodium; Cefonicid Monosodium; Cefonicid Sodium; Cefoperazone Sodium; Ceforanide; Cefotaxime Sodium; Cefotetan; Cefotetan Disodium; Cefotiam Hydrochloride; Cefoxitin; Cefoxitin Sodium; Cefpimizole; Cefpimizole Sodium; Cefpiramide; Cefpiramide Sodium; Cefpirome Sulfate; Cefpodoxime Proxetil; Cefprozil; Cefroxadine; Cefsulodin Sodium; Ceftazidime; Ceftibuten; Ceftizoxime Sodium; Ceftriaxone Sodium; Cefuroxime; Cefuroxime Axetil; Cefuroxime Pivoxetil; Cefuroxime Sodium; Cephacetrile Sodium; Cephalexin; Cephalexin Hydrochloride; Cephaloglycin; Cephaloridine; Cephalothin Sodium; Cephapirin Sodium; Cephradine; Cetocycline Hydrochloride; Cetophenicol; Chloramphenicol ; Chloramphenicol Palmitate ; Chloramphenicol Pantothenate Complex ; Chloramphenicol Sodium Succinate; Chlorhexidine Phosphanilate; Chloroxylenol; Chlortetracycline Bisulfate ; Chlortetracycline Hydrochloride ; Cinoxacin; Ciprofloxacin; Ciprofloxacin Hydrochloride; Cirolemycin ; Clarithromycin; Clinafloxacin Hydrochloride; Clindamycin; Clindamycin Hydrochloride; Clindamycin Palmitate Hydrochloride; Clindamycin Phosphate; Clofazimine ; Cloxacillin Benzathine; Cloxacillin Sodium; Cloxyquin; Colistimethate Sodium; Colistin Sulfate; Coumermycin; Coumermycin Sodium; Cyclacillin; Cycloserine; Dalfopristin; Dapsone ; Daptomycin; Demeclocycline; Demeclocycline Hydrochloride; Demecycline; Denofungin ; Diaveridine; Dicloxacillin; Dicloxacillin Sodium; Dihydrostreptomycin Sulfate; Dipyrithione; Dirithromycin; Doxycycline; Doxycycline Calcium ; Doxycycline Fosfatex; Doxycycline Hyclate; Droxacin Sodium; Enoxacin; Epicillin; Epitetracycline Hydrochloride; Erythromycin; Erythromycin Acistrate; Erythromycin Estolate; Erythromycin Ethylsuccinate; Erythromycin Gluceptate; Erythromycin Lactobionate; Erythromycin Propionate; Erythromycin Stearate; Ethambutol

Hydrochloride; Ethionamide; Fleroxacin; Floxacillin; Fludalanine; Flumequine; Fosfomycin; Fosfomycin Tromethamine; Fumoxicillin; Furazolium Chloride; Furazolium Tartrate; Fusidate Sodium; Fusidic Acid; Gentamicin Sulfate; Gloximonam; Gramicidin; Haloprogin; Hetacillin; Hetacillin Potassium; Hexedine; Ibafloxacin; Imipenem; Isoconazole; Isepamicin; Isoniazid; Josamycin; Kanamycin Sulfate; Kitasamycin; Levofuraltadone; Levopropylcillin Potassium; Lexithromycin; Lincomycin; Lincomycin Hydrochloride; Lomefloxacin; Lomefloxacin Hydrochloride; Lomefloxacin Mesylate; Loracarbef; Mafenide; Meclocycline; Meclocycline Sulfosalicylate; Megalomicin Potassium Phosphate; Mequidox; Meropenem; Methacycline; Methacycline Hydrochloride; Methenamine; Methenamine Hippurate; Methenamine Mandelate; Methicillin Sodium; Metioprim; Metronidazole Hydrochloride; Metronidazole Phosphate; Mezlocillin; Mezlocillin Sodium; Minocycline; Minocycline Hydrochloride; Mirincamycin Hydrochloride ; Monensin ; Monensin Sodium ; Nafcillin Sodium; Nalidixate Sodium; Nalidixic Acid; Natamycin; Nebramycin; Neomycin Palmitate; Neomycin Sulfate; Neomycin Undecylenate ; Netilmicin Sulfate; Neutramycin; Nifuradene; Nifuraldezone; Nifuratel ; Nifuratrone; Nifurdazil; Nifurimide; Nifurpirinol; Nifurquinazol; Nifurthiazole; Nitrocycline; Nitrofurantoin; Nitromide; Norfloxacin; Novobiocin Sodium; Ofloxacin; Ormetoprim; Oxacillin Sodium; Oximonam; Oximonam Sodium; Oxolinic Acid; Oxytetracycline; Oxytetracycline Calcium; Oxytetracycline Hydrochloride; Paldimycin; Parachlorophenol; Paulomycin; Pefloxacin; Pefloxacin Mesylate; Penamecillin; Penicillin G Benzathine; Penicillin G Potassium; Penicillin G Procaine; Penicillin G Sodium; Penicillin V; Penicillin V Benzathine; Penicillin V Hydrabamine; Penicillin V Potassium; Pentizidone Sodium; Phenyl Aminosalicylate; Piperacillin Sodium; Pirbenicillin Sodium; Piridicillin Sodium; Pirlimycin Hydrochloride; Pivampicillin Hydrochloride; Pivampicillin Pamoate; Pivampicillin Probenate; Polymyxin B Sulfate; Porfiromycin ; Propikacin; Pyrazinamide; Pyrithione Zinc; Quindecamine Acetate; Quinupristin; Racephenicol; Ramoplanin; Ranimycin; Relomycin; Repromicin; Rifabutin; Rifametane; Rifamexil; Rifamide; Rifampin; Rifapentine; Rifaximin; Rolitetracycline; Rolitetracycline Nitrate; Rosaramicin; Rosaramicin Butyrate; Rosaramicin Propionate; Rosaramicin Sodium Phosphate; Rosaramicin Stearate; Rosoxacin; Roxarsone; Roxithromycin; Sancycline; Sanfetrinem Sodium; Sarmoxicillin; Sarpicillin; Scopafungin ; Sisomicin; Sisomicin Sulfate; Sparfloxacin; Spectinomycin Hydrochloride; Spiramycin; Stallimycin Hydrochloride; Steffimycin; Streptomycin Sulfate; Streptonicozid; Sulfabenz ; Sulfabenzamide; Sulfacetamide; Sulfacetamide Sodium; Sulfacytine; Sulfadiazine; Sulfadiazine Sodium; Sulfadoxine; Sulfalene; Sulfamerazine;

Sulfameter; Sulfamethazine; Sulfamethizole; Sulfamethoxazole; Sulfamonomethoxine; Sulfamoxole; Sulfanilate Zinc; Sulfanitran ; Sulfasalazine; Sulfasomizole; Sulfathiazole; Sulfazamet; Sulfisoxazole; Sulfisoxazole Acetyl; Sulfisoxazole Diolamine; Sulfomyxin; Sulopenem; Sultamicillin; Suncillin Sodium; Talampicillin Hydrochloride; Teicoplanin; Temafloxacin Hydrochloride; Temocillin; Tetracycline; Tetracycline Hydrochloride; Tetracycline Phosphate Complex; Tetroxoprim; Thiamphenicol; Thiphencillin Potassium; Ticarcillin Cresyl Sodium; Ticarcillin Disodium; Ticarcillin Monosodium; Ticlatone; Tiodonium Chloride; Tobramycin; Tobramycin Sulfate; Tosufloxacin; Trimethoprim; Trimethoprim Sulfate; Trisulfapyrimidines; Troleandomycin; Trospectomycin Sulfate; Tyrothricin; Vancomycin; Vancomycin Hydrochloride; Virginiamycin; and Zorbamycin.

24. The method of claim 14, wherein the anti-fungal agent is selected from the group consisting of imidazoles, FK 463, amphotericin B, BAY 38-9502, MK 991, pradimicin, UK 292, butenafine, chitinase and 501 cream.

25. The method of claim 14, wherein the anti-fungal agent is selected from the group consisting of wherein the anti-fungal agent is selected from the group consisting of Acrisorcin; Ambruticin; Amorolfine, Amphotericin B; Azaconazole; Azaserine; Basifungin; Bifonazole; Biphenamine Hydrochloride ; Bispyrithione Magsulfex ; Butoconazole Nitrate; Calcium Undecylenate; Candicidin; Carbol-Fuchsin; Chlordantoin; Ciclopirox; Ciclopirox Olamine; Cilofungin; Cisconazole; Clotrimazole; Cuprimyxin ; Denofungin ; Dipyrithione; Doconazole; Econazole; Econazole Nitrate; Enilconazole; Ethonam Nitrate; Fenticonazole Nitrate; Filipin; Fluconazole; Flucytosine; Fungimycin; Griseofulvin; Hamycin; Isoconazole ; Itraconazole; Kalafungin; Ketoconazole; Lomofungin; Lydimycin; Mepartricin ; Miconazole; Miconazole Nitrate; Monensin ; Monensin Sodium ; Naftifine Hydrochloride; Neomycin Undecylenate ; Nifuratel ; Nifurmerone; Nitralamine Hydrochloride; Nystatin; Octanoic Acid; Orconazole Nitrate; Oxiconazole Nitrate; Oxifungin Hydrochloride; Parconazole Hydrochloride; Partricin ; Potassium Iodide ; Proclonol ; Pyrithione Zinc ; Pyrrolnitrin; Rutamycin; Sanguinarium Chloride ; Saperconazole; Scopafungin ; Selenium Sulfide ; Sinefungin; Sulconazole Nitrate; Terbinafine; Terconazole; Thiram; Ticlatone ; Tioconazole; Tolciclate; Tolindate; Tolnaftate; Triacetin; Triafungin; Undecylenic Acid; Viridofulvin; Zinc Undecylenate; and Zinoconazole Hydrochloride.

26. The method of claim 1, further comprising administering to the subject an antigen.

27. The method of claim 26, wherein the antigen is a microbial antigen.

28. The method of claim 27, wherein microbial antigen is selected from the group consisting of a bacterial antigen, a viral antigen, a fungal antigen, and a parasitic antigen.

29. The method of claim 1, wherein the antigen is not conjugated to the poly-G nucleic acid.

30. The method of claim 1, wherein the anti-microbial agent is not a cytokine.

31. The method of claim 1, wherein the poly-G nucleic acid has a phosphorothioate modified backbone, and the poly-G nucleic acid is administered systemically.

32. The method of claim 1, wherein the poly-G nucleic acid is free of T-rich motifs and methylated CpG motifs.

33. A method for treating or preventing an infectious disease in a subject having or at risk of developing the infectious disease, comprising

administering to a subject in need of such treatment a CpG nucleic acid and an anti-microbial agent in an effective amount for treating or preventing the infectious disease, wherein the CpG nucleic acid is administered systemically.

34. The method of claim 33, wherein the effective amount is a synergistic amount.

35. The method of claim 33, wherein the anti-microbial agent is administered locally.

36. The method of claim 33, wherein the anti-microbial agent is selected from the group consisting of an anti-bacterial agent, an anti-viral agent, and an anti-fungal agent.

37. The method of claim 33, wherein the CpG nucleic acid is free of T-rich motifs, and methylated CpG motifs.

38. The method of claim 33, further comprising administering to the subject an antigen.

39. The method of claim 38, wherein the antigen is a microbial antigen.

40. The method of claim 39, wherein microbial antigen is selected from the group consisting of a bacterial antigen, a viral antigen, and a fungal antigen.

41. The method of claim 38, wherein the antigen is not conjugated to the CpG nucleic acid.

42. The method of claim 38, wherein the antigen is administered locally.

43. The method of claim 38, wherein the anti-microbial agent is not a cytokine.

44. The method of claim 38, wherein the CpG nucleic acid has a phosphorothioate modified backbone.

45. The method of claim 38, further comprising administering an adjuvant to the subject, provided the anti-microbial agent is selected from the group consisting of an anti-bacterial agent, and an anti-fungal agent.

46. A method for treating or preventing warts in a subject having or at risk of developing warts, comprising,

administering to a subject in need of such treatment, an immunostimulatory nucleic acid in an effective amount for treating or preventing the wart,

wherein the immunostimulatory nucleic acid does not have a phosphorothioate modified backbone.

47. The method of claim 46, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.

48. The method of claim 46, wherein the immunostimulatory nucleic acid is a poly-G nucleic acid.

49. The method of claim 46, wherein the immunostimulatory nucleic acid is a T-rich nucleic acid.

50. The method of claim 46, wherein the immunostimulatory nucleic acid is a non-CpG nucleic acid.

51. The method of claim 46, further comprising administering to the subject an anti-microbial agent.

52. The method of claim 51, wherein the immunostimulatory nucleic acid and the anti-microbial agent are administered in an effective amount to synergistically treat or prevent the wart.

53. The method of claim 51, wherein the anti-microbial agent is an antiviral agent.

54. A method for prophylactically treating a subject at risk of developing the infectious disease, comprising

administering to a subject in need of such treatment an immunostimulatory nucleic acid having a phosphorothioate modified backbone, and an anti-microbial agent in an amount effective to inhibit the infectious disease,

wherein the immunostimulatory nucleic acid is free of a T-rich motif, a methylated CpG motif, and an unmethylated CpG motif.

55. The method of claim 54, wherein the effective amount is a synergistic amount.

56. The method of claim 54, wherein the anti-microbial agent is selected from the group consisting of an anti-bacterial agent, an anti-viral agent, an anti-fungal agent, and an anti-parasitic agent.

57. The method of claim 54, wherein the immunostimulatory nucleic acid is administered systemically.

58. The method of claim 54, further comprising administering an antigen to the subject.

59. The method of claim 58, wherein the antigen is a microbial antigen.

60. The method of claim 59, wherein microbial antigen is selected from the group consisting of a bacterial antigen, a viral antigen, a fungal antigen, and a parasitic antigen.

61. The method of claim 58, wherein the antigen is not conjugated to the immunostimulatory nucleic acid.

62. A method for preventing antibiotic resistance, comprising:

administering to a subject prior to, at the same time as or after the subject has received antibiotic therapy an effective amount of an immunostimulatory nucleic acid for preventing antibiotic resistance.

63. The method of claim 62, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.

64. The method of claim 62, wherein the immunostimulatory nucleic acid is a T-rich nucleic acid.

65. The method of claim 62, wherein the immunostimulatory nucleic acid is a poly-G nucleic acid.

66. The method of claim 62, wherein the immunostimulatory nucleic acid is a nucleic acid having a phosphorothioate backbone modification.

67. The method of claim 62, wherein the immunostimulatory nucleic acid is administered before the antibiotic.

68. The method of claim 62, wherein the immunostimulatory nucleic acid is administered at the same time as the antibiotic.

69. The method of claim 62, wherein the immunostimulatory nucleic acid is administered after the antibiotic.

70. A method for preventing an allergic reaction in a subject receiving an anti-microbial agent, comprising

administering to a subject receiving an anti-microbial agent an immunostimulatory nucleic acid in an effective amount to prevent an allergic reaction to the anti-microbial agent.

71. The method of claim 70, wherein the anti-microbial is selected from the group consisting of an anti-bacterial agent, an anti-viral agent, an anti-fungal agent, and an anti-parasitic agent.

72. The method of claim 70, wherein the anti-microbial agent is an anti-bacterial agent.

73. The method of claim 70, wherein the anti-microbial agent is penicillin.

74. The method of claim 70, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.

75. The method of claim 70, wherein the immunostimulatory nucleic acid is a T-rich nucleic acid.

76. The method of claim 70, wherein the immunostimulatory nucleic acid is a poly-G nucleic acid.

77. The method of claim 70, wherein the immunostimulatory nucleic acid has a phosphorothioate modified backbone.

78. The method of claim 74, wherein the immunostimulatory nucleic acid is administered systemically.

79. A kit comprising

at least one container housing an immunostimulatory nucleic acid, and

at least one container housing an anti-microbial agent, and

instructions for systemic administration of the immunostimulatory nucleic acid,

wherein the immunostimulatory nucleic acid is selected from the group consisting of a CpG nucleic acid, a poly-nucleic acid and a nucleic acid having a phosphorothioate modified backbone.

80. The kit of claim79, wherein the at least one container housing an immunostimulatory nucleic acid is a sustained release vehicle.

81. The kit of claim 79, further comprising instructions for administering the immunostimulatory nucleic acid and the anti-microbial agent in an effective amount for inducing a synergistic immune response in the subject.

82. A composition, comprising:

an immunostimulatory nucleic acid and an antibiotic, formulated in a pharmaceutically-acceptable carrier and in an effective amount for preventing the development of antibiotic resistant strains of bacteria.

83. The composition of claim 82, wherein the antibiotic is selected from the group consisting of broad spectrum antibiotics, narrow spectrum antibiotics, and limited spectrum antibiotics.